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KDHE TB Prevention and Control

12-Dose Isoniazid-Rifapentine TB Infection Treatment Policy

Purpose: This policy describes the selection criteria for appropriate use of 12-Dose Isoniazid-Rifapentine (3HP) regiment for the treatment of Tuberculosis Infection. Furthermore, the policy outlines the process to be used in administration of the regimen as well as interventions to be conducted prior to, during and at completion of treatment.

Background: On December 9, 2011 the Centers for Disease Control and Prevention (CDC) released recommendations on the use of a new treatment regimen for tuberculosis (TB) infection. This new regimen, referred to as 3HP, represents a major advancement in preventing future cases of TB disease and puts us closer to our goal of TB elimination. The 12-dose regimen is a combination regimen of isoniazid and rifapentine given in 12 once-weekly doses under directly observed therapy (DOT). The 12-dose regimen reduces the required treatment for TB infection from 270 daily doses over 9 months to 12 once-weekly doses given over 3 months.

CDC's recommendations are a result of a recent large randomized control trial which found the 12-dose regimen to be as effective for preventing TB as other regimens. The new regimen is also more likely to be completed than the current U.S. standard regimen of 9 months of daily isoniazid given without directly observed therapy. Two additional studies also found the 3HP regimen to be as effective as other regimens in preventing new cases of TB disease. The 3HP regimen does not replace other recommended TB infection treatment regimens; the 3HP regimen is another effective regimen.

The 3HP regimen is NOT recommended for:

Children younger than 2 years of age,
People with HIV/AIDS who are taking anti-retroviral therapy,
Pregnant women or women who expect to become pregnant during treatment, and
People who are presumed to have been infected with isoniazid-resistant or rifampin-resistant *M. tuberculosis*.

The preferred regimen for children aged 2 to 11 years old is 9 months of daily isoniazid.

Medication cost for the new regimen at current Public Health discounted pricing is more than 8 times higher than the most commonly used nine month INH regimen. Cost, however, should not be the only consideration because completion of treatment for TB Infection, especially those at greatest risk for developing TB Disease within their lifetime is the most important factor. Often times, those at greatest risk are also those more likely to not complete treatment under the traditional treatment regimens. The cost of treating an Active TB case which is drug susceptible is estimated to be $17,000 while the cost of treating a multi-drug resistant case of Active TB may be $250,000 or higher.

Policy: Prior to consideration of using any regimen to treat TB Infection, TB Disease must be properly ruled out through use of appropriate diagnostic tools such as Mantoux skin test or IGRA tests, normal chest radiograph, sputum smear and culture results or other tissue smear and culture results and trained provider diagnosis. Note, IGRAs may be required of some candidates. If unfamiliar, inexperienced or unsure of TB diagnosis criteria, expert consultation should be sought through the Kansas Department of Health and Environment TB Prevention and Control Program.

Highest priority populations for use of the 3HP regimen should be targeted to the following groups:

- Recent contacts of active cases.
- High risk patients who may not be in the same county for 9 months.
- High risk patients who have doubtful compliance for a 9 month program.
- Patients who need to start immuno suppressants as soon as LTBI treatment is completed.
- Patients in whom a medical treatment, surgery, or some other important intervention is dependent on completing LTBI.
- Patients considered high risk who are a flight risk.
- Patients who are abusing alcohol or other substances.

Treatment medications will be provided free of charge from the KDHE through local health departments and other licensed providers who agree to full compliance with this policy. Directly Observed Therapy of EVERY dose of treatment is absolutely required. This must be agreed to by the provider and patient prior to starting treatment.

A request for approval to use this regimen through the KDHE may be made through completion and submission of the *Kansas 12-Dose Isoniazid-Rifapentine Enrollment* form (attachment A). KDHE reserves the right to deny request for reasons such as: patient not being in the high priority population list, patient being at risk based on CDC guidelines, unwillingness of provider or patient to comply with DOT requirement or lack of resources to provide the medications.

Once approved for the state supplied regimen, it is expected that the CDC guidelines for best practice be followed. These guidelines are available in the Morbidity and Mortality Weekly published by the CDC on December 9, 2011. For the state supplied regimen, laboratory testing must be taken at baseline (prior to dose one) and at least monthly during treatment. At baseline and monthly according to the tests indicated on the *Laboratory Log and Final Disposition Report*. If HIV status is not documented through testing of twelve months prior or less, an HIV test should be completed at baseline.

Patients are to be educated about the potential side effects of the regimen and instructed to seek medical attention upon the first symptom of a possible adverse event. Providers must maintain and submit upon completion of treatment the *KDHE 3HP DOT Form, KDHE 3HP Laboratory Log and Final Disposition Report* and *KDHE 3HPAdverse Event Report* when applicable (attachments B, C and D) faxed to 785-291-3732 or mailed to TB Prevention and Control, 1000 SW Jackson, Suite 210, Topeka, KS 66612.

Clinical technical assistance questions should be directed to the TB Nurse Consultant at 785-296-0739. Programmatic or policy questions may be directed to the TB Controller at 785-296-8893.

Kansas Department of Health and Environment 12-Dose Isoniazid-Rifapentine TB Infection Treatment Enrollment

Patient Name: _____ **Address:** _____

Date of Birth: _____ **Age:**_____ **Gender:** ☐Male ☐Female ☐Transgender **Ethnicity:** ☐Hispanic ☐Non-Hispanic **Race:** _____

Mantoux Skin Test Result: _____mm **OR IGRA Result:** ☐ Positive ☐Negative ☐Indeterminate **Type of IGRA**: _____

Date of TST or IGRA: _____ **Chest Radiograph Report**: ☐ Normal ☐ Abnormal **Date of Chest Radiograph**: _____

Dose: _____mg **INH**_____mg **RPT** **Weight** _____**kg** **Provider of Treatment:** _____

WORK and ACTIVITY:

Employed ❑No ❑Yes – if yes, type of employment _____

Student ❑No ❑Yes

If yes, is the patient taking an excessive class load or preparing for something like comprehensive exams? ❑No ❑Yes

If yes, has patient been advised of potential fatigue issues ❑No ❑Yes

Sports or other strenuous activities ❑No ❑Yes

If yes, has patient been advised of potential fatigue issues ❑No ❑Yes

If yes, has patient been advised to hydrate well during activities ❑No ❑Yes

MEDICAL RISK FACTORS AND HISTORY:

☐None
☐Diabetes (type) _____
☐Chronic renal disease (☐on dialysis)
☐Immunocompromised (diagnosis_____)
☐Hepatitis (☐B ☐C ☐Other_____)
☐Psychiatric disease
☐Chronic lung disease (☐Silicosis) _____
☐Malnutrition (<10% ideal body weight)
☐Gastrectomy/ jejunoileal bypass
☐Pregnant currently
☐Seizure disorder
☐Mental Health problems _____
☐Alcoholism
☐Current or past smoker (pack-years _____)
☐Other _____
☐None

DOT STATUS:

Have Directly Observed Therapy procedures been agreed to by patient?
❑No ❑Yes

Is the health department or provider committed to Directly Observed Therapy procedures through completion of treatment? ❑No ❑Yes

HIV STATUS:

❑Positive ❑Negative ❑Unknown

If positive, on HART? ❑No ❑Yes

If unknown, when will test be done? _____

BEHAVIORAL RISKS:

Alcohol more than 2 drinks per day: ❑No ❑Yes

IDU drug use: ❑No ❑Yes (state)_____

Non-IDU drug use: ❑No ❑Yes (state)_____

REFUGEE or IMMIGRATION STATUS:

Refugee or Immigrant: ❑No ❑Yes (Date of U.S. arrival _____) TB Classification upon arrival: ❑No ❑Yes (Classification _____)

Country(ies) of birth or extensive travel _____

Patient Name: _____

POPULATION RISK FACTORS DURING LAST 12 MONTHS:
(√ all that apply):

- ❑Homeless or SRO/Shelter resident
- ❑Incarcerated (prison, jail, juvenile hall)
- ❑Long-term care facility resident
- ❑Health care worker
- ❑Migrant worker
- ❑Homeless shelter employee
- ❑Correctional facility employee
- ❑Other high-risk setting employee_____

PREGNANCY RISKS (FEMALES ONLY):

Is patient pregnant: ❑No ❑Yes

(If yes, this treatment regime may not be used)

Is patient on birth control? ❑No ❑Yes

If yes, method _____

Could patient become pregnant during treatment: ❑No ❑Yes

If yes, has patient been educated of risk and advised to alert provider if there is a possibility she has become pregnant so that medication can be stopped immediately: ❑No ❑Yes

OTHER MEDICATIONS CURENTLY TAKEN (OR RECENTLY DISCONTINUED):

Class of Drugs		**Name and Dose of Medication**	**Start Date**	**Stop Date (if applicable)**
Phenytoins (anti-seizure)	❑No ❑Yes			
Anti-depressants or anti-psychotics	❑No ❑Yes			
Methadone	❑No ❑Yes			
Theophylline	❑No ❑Yes			
Calcium channel blockers (blood pressure med) (verapamil, diltiazem, amlodipine, nifedipine)	❑No ❑Yes			
Warfarin (blood thinner)	❑No ❑Yes			
Statins (cholesterol-lowering drugs)	❑No ❑Yes			
TNF-α inhibitors (ertanecept, adalimumab, infliximab, golimumab, pegsunercept, certolizumab)	❑No ❑Yes			
Other	❑No ❑Yes			
Other	❑No ❑Yes			

BASELINE LABORATORY RESULTS REQUIRED FOR TREATMENT PROGRAM ADMISSION:

Liver function tests	Result	Complete Blood Count	Result	Chemistry Panel	Result
Date (mm/dd/yyyy)		Date (mm/dd/yyyy)		Date (mm/dd/yyyy)	
AST (0 – 35 U/L)		Hemoglobin (Male: 14 – 17 g/dL, Female: 12 - 16 g/dL)		Na (Sodium) (136 – 350 meq/L)	
ALT (0 – 35 U/L)		Hematocrit (Male: 41% - 51%, Female: 36% - 47%)		K (Potassium) (3.5 - 5.0 meq/L)	
Alk Phos (36 – 92 U/L)		White Blood Cell Count ($4.0 – 10 \times 10^9$ /L)		BUN (urea nitrogen) (8 – 20 mg/dL)	
T. Bili (0.3 - 1.2 mg/dL)		Platelets ($150 – 350 \times 10^9$ /L)		Cr (Creatinine) (0.7 – 1.3 mg/dL)	
(Other) _____		(Other) _____		(Other) _____	

Patient Name: _____

Isoniazid and Rifapentine Shipment Request: (medications will only be sent to local health departments or medical care providers who agree to provide Directly Observed Therapy for each of the twelve doses. Medications should be shipped to:

Contact Name: _____ _____

Agency: _____ Address: _____

Phone: _____ Address (line 2)__ _____

Please fax completed data to: Kansas TB Control and Prevention (785) 291-3732 prior to start of treatment.
Medications will be supplied free of charge upon receipt of initial data form completion.

KDHE Use Only:

Clinical review completion date: _____ by _____

Note any clinical contraindications:_____

_____

TB Controller Review for approval:

☐**Approved** ☐ **Not Approved (if not approved, explain below)**

_____

_____

_____

KDHE TB Controller **Date**

Form updated 8/8/12

DIRECTLY OBSERVED THERAPY LOG
12-Dose Isoniazid-Rifapentine Latent TB Infection Treatment

Patient Name: _____ Date of Birth: _____
Initial Weight _____kg Dose: _____mg INH_____mg RPT

Date: Dose:	__/__ __1__	__/__ __2__	__/__ __3__	__/__ __4__	__/__ __5__	__/__ __6__	__/__ __7__	__/__ __8__	__/__ __9__	__/__ __10__	__/__ __11__	__/__ __12__
Loss of Appetite	□	□	□	□	□	□	□	□	□	□	□	□
Nausea or vomiting	□	□	□	□	□	□	□	□	□	□	□	□
Yellow eyes or skin	□	□	□	□	□	□	□	□	□	□	□	□
Diarrhea	□	□	□	□	□	□	□	□	□	□	□	□
Rash or hives	□	□	□	□	□	□	□	□	□	□	□	□
Fever or chills	□	□	□	□	□	□	□	□	□	□	□	□
Sore muscles	□	□	□	□	□	□	□	□	□	□	□	□
Numbness or Tingling	□	□	□	□	□	□	□	□	□	□	□	□
Fatigue	□	□	□	□	□	□	□	□	□	□	□	□
Dizziness/fainting	□	□	□	□	□	□	□	□	□	□	□	□
Abdominal pain	□	□	□	□	□	□	□	□	□	□	□	□
Other _____	□	□	□	□	□	□	□	□	□	□	□	□
Rx stop or held (complete adverse reaction log)	□	□	□	□	□	□	□	□	□	□	□	□
No adverse reaction	□	□	□	□	□	□	□	□	□	□	□	□
Current Weight	kg	kg	kg	kg	kg	kg	kg	kg	kg	kg	kg	kg
Blood Pressure	/	/	/	/	/	/	/	/	/	/	/	/
Provider Initials*												

***** Printed name for initials: ____ _____ | ____ _____ | ____ _____
Initials Printed name Initials Printed name Initials Printed name

Updated 8/8/12

Patient Name: _____

Laboratory Log and Final Disposition Report
12-Dose Isoniazid-Rifapentine Latent TB Infection Treatment

If levels are abnormal, please include level and notify State TB Nurse immediately at 785-296-0739. Labs must be drawn at least monthly during treatment. Copies of the lab reports are to be sent with the completion of treatment along with all treatment logs.

	Date	Date	Date	Date	Date	Date	Date	Date
LFT (AST, ALT, Alk Phos, T. Bili)	□normal □abnormal _____	□normal □ abnormal _____	□normal □abnormal _____	□normal □abnormal _____	□normal □abnormal _____	□normal □abnormal _____	□normal □abnormal _____	□normal □abnormal _____
CBC (Hemoglobin, Hematocrit, WBC, PLT CT)	□normal □abnormal _____	□normal □abnormal _____	□normal □abnormal _____	□normal □abnormal _____	□normal □abnormal _____	□normal □abnormal _____	□normal □abnormal _____	□normal □abnormal _____
Metabolic (Na, K, BUN, Creatinine)	□normal □abnormal _____	□normal □abnormal _____	□normal □abnormal _____	□normal □abnormal _____	□normal □abnormal _____	□normal □abnormal _____	□normal □abnormal _____	□normal □abnormal _____

Final Disposition: □Completed treatment □Stopped treatment □ adverse event □ lost to f/u □ moved □ other

Final Disposition Date: _____

Please fax or mail the following upon final disposition of the treatment:
Kansas TB Control and Prevention
1000 SW Jackson, Suite 210
Topeka, KS 66612
Fax: (785) 291-3732

Final Disposition Check List to send to KDHE:

- ☐ **Directly Observed therapy log**
- ☐ **Adverse Event Episode Report (if applicable)**
- ☐ **Laboratory Log**
- ☐ **Copies of monthly laboratory reports**

Updated 8/8/12

Patient Name: _____

Adverse Event Episode Report
12-Dose Isoniazid-Rifapentine Latent TB Infection Treatment

Please complete for any adverse event which causes interruption in therapy.

Date	Symptom Onset	Symptom Duration	Hospitalized	# doses taken	Re-challenge	Outcome	Diagnosis
	□ < 2 hrs □ 2-48hrs □ >48hrs	□ < 1 day ___hrs □ ≥ 1 day __days	□ yes □ no		□ yes □ no (skip to diagnosis)	□ Continue Rx □ INH intolerant □ RPT intolerant	□ Hepatitis* □ Allergic reaction □ Systolic BP less than 90 mm Hg □ Rash □ Other_____ □ None

*3x upper level of normal if symptomatic, 5x upper level of normal if asymptomatic

Liver function test	Result	Complete Blood Count	Result	Chemistry Panel	Result
Date		Date		Date	
AST		Hemoglobin		Sodium	
ALT		Hematocrit		Potassium	
Alk Phos		WBC		BUN	
Total Billi.		Platelets		Creatinine	
Other (specify)		Other (specify)		Other (specify)	

Comment: Please briefly describe the adverse event, including symptoms, time of onset in relation to last INH-RPT dose, duration and resolution and any other related factors (other medical conditions, medications).

Updated 8/8/12